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Dr. Ashwin R Dangi

Associate Professor,

Department of Pediatrics,

Nootan Medical College and

Research Centre. Sakalchand

Patel University. Visnagar,

Gujarat, India

Dr. Jayant R Salvi

Assistant Professor,

Department of Pediatrics,

GMERS Medical College,

Dharpur, Patan, Gujarat,

India

Incidence and risk factors of hypoglycemia among neonates: A prospective study

Dr. Ashwin R Dangi and Dr. Jayant R Salvi

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Abstract

Background and Aim: It has been observed that low levels of the blood glucose do not cause health issues in the neonates. This is due to the fact that the neonates are adjusting to the life outside the uterus. Present study was carried out to study incidence and risk factors of hypoglycemia among neonates in semi urban areas.

Material and Methods: This was a hospital based prospective study performed at the Department of Pediatrics, Nootan general hospital NMCRC Visnagar, India January 2021 to June 2021. 150 neonates were included. Ballard's score was used to divide them into four groups of gestational age. Standard glucometer was used to measure blood glucose in mothers and neonates. For mothers, it was measured at time of delivery. For neonates, it was measured at zero, three, six, twelve and twenty four hours of birth. Standard treatment protocol was followed for neonatal hypoglycemia

Results: As the mother blood glucose increased the babies blood glucose decreased with $r=-0.18$ but this correlation was not found to be statistically significant ($p>0.05$). The differences in the blood glucose levels at different time points at different gestational ages were not found to be statistically significant. As maternal blood glucose increased, neonatal glucose decreased. Important risk factors found for hypoglycemia in neonates were being born by lower segment cesarean section (LSCS), low for gestational age (LGA) babies and small for gestational age (SGA) babies, pre-term and post term babies. But these risk factors were not found to be statistically significant ($p>0.05$).

Conclusion: Hypoglycemia is surprisingly common among neonates in developing countries. There was a wide variation of blood glucose levels in newborns. Preterm and post-term babies, babies delivered by LSCS, LGA and SGA babies were more prone for hypoglycemia requiring blood glucose monitoring.

Keywords: Blood glucose, hypoglycemia, lower segment cesarean section, low for gestational age

Introduction

For normal functioning of the brain cells, most necessary is glucose. Hypoglycemia can lead to damage to the brain. This can be taken care by appropriate and adequate treatment. Adequate neurological development in the neonates is ensured by normal blood glucose. This correlation has been shown in different studies [1]. Proper gluconeogenesis ensures that the normal blood glucose is achieved. Risk factors for impaired gluconeogenesis are mother with diabetes, SGA, pre-term babies and LGA. Hence early diagnosis and treatment of hypoglycemia in these high risk groups are required to prevent the complications [2-4].

Neonatal hypoglycemia is one of the common metabolic abnormalities encountered in neonatal medicine [5-7]. Soon after birth, from 3% to as much as 29% babies encounter hypoglycemic condition [8-11]. It occurs frequently as a transient disorder, particularly in premature and small-for-gestational-age infants and if not treated promptly, it may lead to significant neurologic consequences, such as seizures and permanent brain damage or death [4, 12-16].

The fetus does not accumulate glycogen until after 27 weeks' gestation, with a slow continual increase until after 36 weeks' gestation, and a rapid accumulation to reach 50 mg/g of tissue by term [17]. After birth, the glucose concentration decreases to a nadir of 3-3.3 mmol/L in the first 1-2 h in term infants. Term infants use the stored glycogen for self-sufficient glucose homeostasis.

Various factors like weight at birth, comorbidities at birth, complications that may occur during perinatal period, gestational age, behavior of the mother during feeding of the baby [8-10]. One study has reported that the 16% was the hypoglycemia incidence among babies who were LGA [12]. The incidence varies if the cut-off point varies.

Corresponding Author:

Dr. Jayant R Salvi

Assistant Professor,

Department of Pediatrics,

GMERS Medical College,

Dharpur, Patan, Gujarat,

India

For cutoff point of <1.7 mmol/l (30.6 mg/dl) it is 8.1% compared to 20.6% for cut-off point of < 2.2 mmol/l (39.6 mg/dl) [10].

Generally it has been observed that low levels of the blood glucose do not cause health issues in the neonates. This is due to the fact that the neonates are adjusting to the life outside the uterus [18, 19]. But if this variation is of chronic nature, then it may be associated with the complications. Chronic hypoglycemia in neonates is associated with brain injury [20]. Appropriate for gestational age (AGA) babies may not require monitoring of blood glucose. But we have no idea on how asymptomatic hypoglycemia is present in these babies and if not attended may lead to brain damage. There is also no clarity on when and how frequently the blood glucose should be monitored. This particular aspect is not much studied in the available literature. If the mother is diabetic, then the asymptomatic hypoglycemia is common in the babies born to such mothers [21].

As screening the blood glucose of all the babies is not feasible in resource-poor set-up, identifying the risk factors of neonatal hypoglycemia is critical to find out the infants 'at risk' in order to reduce their morbidity and mortality by appropriate timely intervention.

Present study was carried out to study incidence and risk factors of hypoglycemia among neonates in semi urban areas.

Material and Methods

This was a hospital based prospective study performed at the Department of Pediatrics, Nootan general hospital NMCRC Visnagar, India January 2021 to June 2021. Stark *et al.* found that the incidence of hypoglycemia among newborns was 27%.²⁰ Sample size came out to be 145 with 95% confidence interval. Total round up sample size was up to 150.

Babies born at the study center during the study period were included in the study. Exclusion criteria included neonates with major congenital anomalies or conditions that might adversely affect breathing or ventilation.

Ethical approval was taken from the institutional ethical committee and written informed consent was taken from all the participants.

Ballards score was used to divide them into four groups of gestational age. For division using weight for gestational age, charts from Seton medical centre, Austin were used.²³ Accu-Chek performa made by Roche diagnostics, Mannheim, Germany was used for monitoring the blood glucose levels. It was standardized as per the standard guidelines. All aseptic precautions were taken while taking the blood sample not only from mothers but also from neonates. From mothers, the sample was collected either at the time of delivery or within 30 minutes of delivery. From neonates, the sample was collected at zero hour, three hours, six hours, twelve hours and twenty four hours of birth. Mothers were trained in breast feeding practices before initiating the breast feeding to their babies as per the baby friendly hospital initiative policy. If the blood glucose was found out to be less than 40 mg/dl, they were examined in

detail to look for the signs of hypoglycemia. In all these cases, breast feeding was continued and monitoring of the blood glucose was done.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

Table 1 shows distribution of study subjects as per different parameters. Male babies were more than female babies (87 versus 63). 76 were delivered by LSCS. 81 were primiparous mothers. 98 babies were born at the gestational age of 38-40 weeks. As the time duration from birth increased, the mean blood glucose levels increased from 2.96 at birth zero hours to 3.80 at 24 hours after birth.

As the mother blood glucose increased the babies blood glucose decreased with $r=-0.18$ but this correlation was not found to be statistically significant ($p>0.05$). The differences in the blood glucose levels at different time points at different gestational ages were not found to be statistically significant ($p>0.05$).

The blood glucose levels of the neonates born vaginally were more than those babies who were delivered by LSCS. But this difference was not statistically significant at any point of time ($p>0.05$). The blood glucose levels of LGA neonates were lower at zero levels compared to SGA and AGA babies. At three hours, six hours the SGA babies had low mean blood glucose compared to other two. At 12 and 24 hours, the AGA babies had low mean blood glucose levels. But none of these differences were found to be statistically significant ($p>0.05$). The incidence of Hypoglycemia was 17.3% at birth which reduced to 10.6% three hours to around seven percent at six hours and around one percent at 12 and 24 hours. This reduction was due to some babies who got corrected on their own and some became normal after treatment.

Table 1: Distribution of study subjects as per different parameters.

Variables	Number	Percentage
Gender		58
Male	87	42
Female	63	
Mode of delivery		
Vaginal	74	49
LSCS	76	51
Parity of Mother		
Primiparous mother	81	54
Multiparous mother	69	46
Gestational age at which babies were born (weeks)		
34-36	6	4
36-38	30	20
38-40	98	72
40-42	6	4

Table 2: Effect of gestational age on variation in blood glucose levels

Time interval	Gestational age (in weeks)	N	Newborn blood glucose (mmol/l) mean+SD	P value
0	34-36	6	2.70+0.75	0.45
	36-38	30	2.84+0.56	
	38-40	98	2.97+0.89	
	40-42	6	2.52+0.51	
3 rd	34-36	6	3.85+2.01	0.1
	36-38	30	3.29+0.54	
	38-40	98	3.46+1.04	
	40-42	6	3.12+0.73	
6 th	34-36	6	4.19+2.02	0.24
	36-38	30	3.27+1.01	
	38-40	98	3.34+1.15	
	40-42	6	3.14+0.54	
12 th	34-36	6	3.72+0.63	0.32
	36-38	30	3.61+0.89	
	38-40	98	3.64+1.09	
	40-42	6	4.06+0.45	
24 th	34-36	6	4.06+0.49	0.47
	36-38	30	3.96+0.92	
	38-40	98	3.70+0.79	
	40-42	6	3.24+0.46	

Test applied one way ANNOVA

Table 3: Incidence of hypoglycemia at different time intervals

Time intervals (in hours)	Number of babies with hypoglycemia	%
At Birth	26	17.3
3	16	10.6
6	11	7.3
12	2	1.3
24	1	0.6

Discussion

As the maternal blood glucose increased, the neonatal blood glucose decreased. Mother with high blood glucose levels at delivery had babies with low glucose levels. Singhi *et al.* also reported the similar negative correlation between maternal blood glucose levels and neonatal blood glucose levels [24]. Curet *et al.* also noted that the incidence of hypoglycemia in neonates was less among those neonates whose mother blood glucose was lower before and during delivery compared to those neonates whose mother blood glucose was higher before and during delivery [25]. Mendiola *et al.* observed that the incidence of hypoglycemia was significantly associated with blood glucose levels of mother [26].

We observed that as the period from birth increased, the average blood glucose levels also increased. Cornblath *et al.* found that there was a small decrease in the mean blood glucose levels of the neonates in the first few hours and then the mean blood glucose levels started to increase [27].

Gestational diabetes mellitus and maternal BMI at delivery were found to play a significant role in the development of hypoglycemia in our study. Other studies had also found significant relationship among these variables [7, 8, 9].

We found that the minimum blood glucose value was 24 mg/dl and the maximum was 140 mg/dl. Thus there was a wide variation in the blood glucose in the neonates in the present study. Hawdon *et al.* also noted from their study that the minimum blood glucose was 24 mg/dl and the maximum blood glucose level was 219.6 mg/dl [28]. Hawdon *et al.* also noted from their study that the minimum blood glucose was 24 mg/dl and the maximum blood glucose level was 219.6 mg/dl [28].

In the present study, babies with gestational age of 34-36

weeks and 40-42 weeks have shown lower blood glucose levels which increased in babies with 34-36 weeks of gestational age at three hour and lower in 40-42 weeks gestational age babies. Hawdon *et al.* observed that the mean blood glucose levels were low in babies born pre term compared to the term babies [28]. Kayiran *et al.* also reported more incidence of hypoglycemia in pre-term babies compared to term babies [29]. Infants of diabetic mothers are more likely to be LGA and they have been previously reported to be associated with neonatal hypoglycemia, although this population was predominantly term infants [30, 31]. Therefore, while LGA infants did not demonstrate significant increase in risk of hypoglycemia in our population, and significance of SGA infants was unable to be completed due to sample size. Further studies with a larger number of infants might yield different results.

In the present study, the incidence of hypoglycemia was 17.3% at birth which reduced to 10.6% three hours to seven percent at six hours and one percent at 12 and 24 hours. This reduction was due to some babies who got corrected on their own and some became normal after treatment. The incidence of hypoglycemia was 15.15% carried out at Tehran children's hospital of Iran [32]. It was 10% in a study which was done in Philadelphia [33]. Study at Kilifi district hospital in Kenya found an incidence of 23% which is more than that we found in the present study [34]. James-Todd *et al.* reported an overall incidence of 41% in infants < 32 weeks' gestation, however, they used point of care glucose measurements which have poor sensitivity in the hypoglycemia range and also excluded infants of diabetic mothers [35, 36]. Harris *et al.* reported an incidence of 51% in infants ≥ 35 weeks' gestation within the first 48 h after birth [37]. A recent study reported that the nadir of plasma glucose

concentration in preterm infants and extremely preterm infants is after 70.5 and 60.9 min, respectively^[36].

We observed that the signs of hypoglycemia were seen in 9% of the cases at birth which decreased to 7% at three hours of birth and further reduced to 6% at six hours and again decreased to 1% at 12 and 24 hours of birth. Haworth *et al.* enlisted few major signs of hypoglycemia in their study such as apnea, cyanosis, irritability, lethargy, muscular twitching, convulsions, poor sucking and disappearance of grasp and other reflexes^[38]. Other studies done by Depuy *et al.* Duvanel *et al.* also support these variables for their connection with neonatal hypoglycemia^[39, 40]. Several reports showed that blood glucose level can increase after feeding in case of transient hypoglycemia.⁴¹ It suggests that timely feeding after birth can also reduce the incidence of neonatal hypoglycemia.

Conclusion

Hypoglycemia is surprisingly common among neonates in developing countries. There was a wide variation of blood glucose levels in newborns. Preterm and post-term babies, babies delivered by LSCS, LGA and SGA babies were more prone for hypoglycemia requiring blood glucose monitoring.

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